



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

MEMORANDUM

SEP 29 1982

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

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9/15/82

SUBJECT: Review Article Entitled An Assessment of the Potential Inhalation Hazard Associated with the Use of Paraquat by L. L. Smith and M. S. Rose; Imperial Chemical Industries Limited, Central Toxicology Laboratory, Alderley Park, Macclesfield, Cheshire, U. K. Report No. CTL/P/646, dated 7/24/81.

EPA Accession No. 246629
EPA Record No. 57 894
TOX Chem. No. 634

Submitted by: Chevron Chemical Company
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This submission should be placed in the Toxicology Branch /HED paraquat file, but it adds little to what many of us already know about the inhalation toxicity of paraquat. It does not close, also, the existing data gaps in the acute and subchronic inhalation toxicity studies. Its main value lies, probably, in the listing of references from the open literature where original data can be obtained, especially by those who had little or nothing "to do with paraquat".

This submission is based on 30 publications, 27 of which appeared in the open literature. Most of the papers (24) were published in 1971-1981. Most of the data quoted in detail was already evaluated by Toxicology Branch/HED (EPA Accession Nos.: 241187, 241188, 241189 and 243856). This submission consists of the following sections:

- A. Summary
- B. Introduction
- C. The effects of paraquat on the lungs of experimental animals and man.
- D. The relationship between morphological damage and paraquat levels in the lungs of rats
- E. Epidemiological effects
- F. References

The following points are of interest in this submission:

1. Agricultural spraying of paraquat, in order to impact upon the target vegetation, does not generate significant quantities of respirable particles. The exposure of the lung by inhalation of the spray can, therefore, be considered negligible.
2. The no-effect level for the morphological lung damage in the rat is 0.1 ug of paraquat ion/l, based on a 3-week inhalation study (5 days/week; 6 hrs/day; EPA Accession No. 241188). Reviewer's Note: This NOEL for the specific organ, the lung, should be distinguished from the overall NOEL which is 0.01 ug of paraquat ion/l and is based on the same 3-week inhalation study.
3. The primary event in the development of lung lesions in rats is the damage to the alveolar epithelium and it occurs within a day of dosing with paraquat. Rats that survive this early acute damage develop proliferative fibrosis.
4. Paraquat accumulates in the alveolar epithelium of the lungs of both rat and man. Lung damage following the ingestion of paraquat is similar histopathologically in both rat and man. It is generally accepted that the rabbit lung is much less sensitive to paraquat than the rat lung both by systemic and inhalation routes.

5. Rat lungs "can tolerate levels of paraquat up to 1 ug/g of tissue for considerable periods of time without developing any morphological evidence of damage".

- a. In one study (EPA Accession No. 241189), 0.1 ug of paraquat ion was instilled directly into the left lobe of the lungs of rats and the animals were killed after 2 or 14 days following the single instillation. Since the lobe weighed about 300 mg, it was concluded that 0.3 ug of paraquat/g of wet lung tissue did not cause acute damage.
- b. In another study (EPA Accession No. 243856) rats were exposed to 0.1 ug of paraquat ion/l for 3 weeks (5 days/week; 6 hrs/day). Paraquat levels rose to about 1.3 ug/g of wet lung tissue after the fifth exposure and remained at that level for the duration of the test. When exposure was discontinued, the levels of paraquat in the lungs decreased with a half-life of 2 days. According to this submission (p. 6), "Since the detailed examination of the lungs of these animals revealed no evidence of morphological damage, it can be concluded that rat lung can tolerate levels of paraquat of between 1 and 2 ug/g of lung without adverse effects for up to 3 weeks".

Reviewer's Note: Neither gross necropsy nor histopathology was performed in that study (EPA Accession No. 243856). This conclusion was based on the results of another study with rats (EPA Accession No. 241187), where a 3-week exposure to 0.1 ug of paraquat ion/l did not show any morphological evidence of damage to the lung.

It is also unclear where the levels ".....of between 1 and 2 ug/g of lung....." come from. According to the study quoted in this submission (EPA Accession No. 243856), rats can tolerate up to 1.3 ug of paraquat/g of lung for at least 3 weeks without sustaining damage. Paraquat level of 2 ug/g of rat lung was observed at the exposure level of 0.5 ug/l in the same study, but there was lung damage at that level.

- c. Rats ingesting 150 ppm of paraquat for 12 months had levels of paraquat approaching 0.5 ug/g of lung and no lung damage.

Reviewer's Note: Toxicology Branch/HED is unfamiliar with that study.

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*W. H. O. S. P.
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